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Thesis

RECENT ADVANCES IN THE MORPHOLOGY AND PHYSIOLOGY OF THE VEINS

by

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RECENT ADVANCES IN THE MORPHOLOGY AND PHYSIOLOGY OF THE VEINS

The veins have been largely neglected by investigators of the vascular system. The anatomists have taken little interest in such variable structures; the physiologists have regarded the veins as passive tubes of less importance than the more dynamic forces of the heart and arteries. The fact that clinicians and physiologists have for long been content with the concept of a vein as a passive channel, partly accounts for the apparent lack of interest in venous pathology.

Only a few investigators have made comprehensive studies of the venous system. Of these investigators, Hooker, 1914, examined the structure of the venous vessels; Eyster, 1926, made a survey of the factors influencing venous pressure; and Franklin, 1928, studied the physiology of the veins. Several have dealt briefly with the veins, but usually in conjunction with other branches of investigation.

Since all the written accounts of recent advances in morphology and physiology of the veins are widely dispersed, it is the intent of this study to re-examine and combine these recordings.

MORPHOLOGY OF THE VEINS

A. DEVELOPMENT OF THE VEINS

Franklin, 1928, stated that blood vessel development was dependent upon both inherited and functional factors. The former account for the disappearance of certain embryonic veins, and for the peculiar structure of the venous system, e.g. the corpora cavernosa, retia mirabilia. The latter come into play shortly after the beginning of functional activity and are related to the needs of the parenchyma of the organ concerned. Functional differences in pressure determine the difference in structure of the venous and arterial walls. The width of the veins is also functionally determined. Circular and longitudinal musculature develop where it is necessary to prevent dilation or longitudinal stretching. Circular muscle is absent in veins which are protected by surrounding tissue, as in the bones and brain.

In 1939, Clark observed the growth of capillaries and veins. He stated that the exact mode of embryonic development of blood vascular endothelium has not been definitely established for all classes of vertebrates; yet there is a general agreement that, after a brief period of differentiation, the growth of the vascular

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system is accomplished by the sending out of endothelial sprouts which anastomose with neighboring sprouts to form a primitive capillary network. Early investigators, Arnold, 1871, Rouget, 1873, observed directly the formation of capillary sprouts from preëxisting endothelium in the living animal in the transparent tails of amphibian larvae.

Sandison, 1928, made studies of the growth of the blood vessels in transparent chambers showing that the new vessels appeared as capillary extensions from preëxisting, functional vessels. Circulation through the newly formed network was established by the differentiation of the new capillaries into arteries and veins. In some cases, the new vessels retracted and disappeared.

The development of methods for inserting permanent transparent chambers into rabbits' ears (Clark, 1930, Abell and Clark, 1932) made it possible to observe the process of new growth of tissue, microscopically, in the living mammal. Clark, 1939a, studied this development in round table chambers inserted into the ears of rabbits. He verified the findings of Sandison by showing that new blood vessels occur by means of endothelial sprouts which anastomose to form loops. The loop formation continues until the growing zone advances across the table space. Older portions of the new network show a beginning of differentiation of vessels into arterioles and venules. This process continues until the whole space is covered by a vascular plexus. Like Sandison, he also

noticed that vessels receiving a small flow grew smaller, retracted and disappeared.

In 1934, Clark also observed the formation of new arterio-venous anastomoses. Their origin was traced to the arterial-venous capillary loops of the primitive growing plexus found in embryos and in regenerating areas of the adult mammal. He discovered that a new arterio-venous anastomosis formed within a few days from small vessels already present in the vascular plexus. This was done by enlarging of the lumen, straightening of their courses and thickening of their walls. This thickening was accomplished by the addition of extra-endothelial cells resembling the smooth muscle cells on the arterioles.

Microscopic observations on the mode of formation, fate, and behavior of extra-endothelial cells on living mammalian blood vessels were made by Clark, 1940, by use of the transparent chambers. He found that adventitial cells developed from connective tissue cells on mammalian capillaries like those on amphibian vessels. Fibroblast-like cells were observed to flatten out on the walls of new blood vessels, and assume a longitudinal arrangement with the vessel wall. The number of adventitial cells seem to vary with the number of fibroblasts present in the region on the growing vessel. If the vessel remains a capillary, these cells increase slightly, retaining their longitudinal arrangement. About some of the larger veins, a capsular arrangement of fine connective tissue fibrillae form outside the layer of adventitial cells.

THE UNIVERSITY OF CHICAGO

DEPARTMENT OF CHEMISTRY

PHYSICAL CHEMISTRY

LECTURE NOTES

BY

PROFESSOR

JOHN D. COLEMAN

CHICAGO, ILL.

1960

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The investigators have been puzzled as to the factors responsible for the formation of new vessels. On the basis of experiments made by Clark and others, it appears that new vessels will grow in an environment of proper physical condition. Some physical factors influencing growth are: temperature conditions, components of surrounding medium, and possibly an increase in blood flow or increase in the amount of interchange through the capillary walls.

B. MACROSCOPIC ANATOMY OF THE VEINS

SYSTEMS OF THE VEINS

Salter, 1852, divided the veins into four systems, the systemic and portal which carry venous blood, and the pulmonary and some veins peculiar to vetal life, e.g. ductus venosus and umbilical veins, which carry arterial blood. Parts of the venous system are modified. In some animals, the vena cava had an extra amount of fibrous tissue at the point of intersection with the diaphragm. Some mammals have veins joining the heart which are invested with a layer of muscle of cardiac type. Other peculiarities may be found in the structure of the umbilical veins as well as in the cerebral sinuses which lack the muscular elements of a typical coat.

A study was made of the anterior cardiac veins by Gregg, 1943, with particular emphasis placed on their functional importance in the venous drainage of the right heart. His studies showed that the coronary vascular system had two pathways for venous drainage. The first, was the superficial or subepicardial venous system, consisting primarily of the anterior cardiac veins and the coronary sinus entering the right atrium. The second was the deeper system of veins which are connected directly with the

chambers of the heart. Functional significance of these pathways has led to extensive physiological study. It was once believed that all coronary blood was drained by the coronary sinus, but it has been shown since then that the Thebesian vessels aid in coronary blood drainage. Other investigators have shown that the Thebesian vessels drain nearly all of the right heart and the left ventricular myocardium is drained primarily by the coronary sinus.

Gregg, 1943, studied the anatomical distribution of the anterior cardiac veins in the heart of a dog (injected postmortem). He found that the subepicardial surface of the right ventricle was covered by many small vessels which converge into two to five major anterior cardiac veins. These cardiac veins empty into the right atrium. By observing several anesthetized dogs, he found that the major portion of the right coronary inflow drained by way of the anterior cardiac veins into the right atrium. This disproves the original belief that nearly all the right coronary inflow drains by way of the Thebesian vessels into the right ventricle.

The venous renal circulation has been studied but little. Morison, 1926, studied the human kidney. He observed that the venous radicles and trunks resemble the accompanying arteries, but differ in that the venous vessels anastomose freely. In the human

kidney, he found that the cortex corticis (the subcapsular zone) consisted of a superficial venous system. In the dog this system was more amplified and in the cat the system was amplified even to a larger degree.

Cerebral circulation has been investigated rather extensively, though little emphasis has been placed on the venous aspect. According to Baily, 1934, the cerebral veins are divided into two groups, the internal and the external, with anastomoses between them which are incomplete. He stated that the internal group drains the great cerebral vein of Galen and the external group comes from the region of the insula.

Some observations were made of the cerebral veins by Stopford, 1930. His efforts proved that the direction of the terminal portion of the great veins is altered because growth produces an interior displacement of the frontal lobe. This causes the anterior veins to be directed posteriorly and the posterior veins course obliquely anteriorly as they pass to the superior sagittal sinus. These sinuses drain into channels at the base of the skull.

Forbes, 1928, studied the pial vessels, placing his attention upon the movement of the corpuscles. The flow in the minute vessels appeared slower and steadier, while in the veins it was more rapid and even so rapid that the corpuscles were no longer visible.

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VALVES OF THE VEINS

A considerable amount has been written about the valves of the venous system since they were first discovered, but there are many discrepancies in descriptions given in standard anatomical texts. Trent, 1944, stated that William Harvey discovered circulation by observing the valves of the veins. He noticed that the valves in the veins of many parts of the body were so placed that they gave free passage to the blood towards the heart, but opposed the passage of the venous blood the contrary way. This led him to believe that nature had not placed the valves without design. To him no design seemed more probable; since the blood could not flow through the veins to the limbs because of the interposing valves, it must, therefore, be sent through arteries and return through veins whose valves did not oppose its course.

Kampmeier, 1926, made a study of the venous valves. He first considered the vessels of the head and the neck and confirmed the belief that the sinuses invariably are valveless. This holds true also of their tributaries, the ophthalmic, meningeal, cerebral, and diploic veins. The emissary veins, particularly the parietal one joining the superior sagittal sinus and the veins of the scalp, do not possess valves directed peripherally. The tributaries of

the internal jugular, superior thyroid, facial, lingual and the temporal veins, all bear valves at their mouths. At the entrance of the deep cervical vein into the vertebral vein, there is a valve, either unicuspid or bicuspid in type. Another is found at the point of junction of the vertebral vein with the innominate vein. We find that the vessels of narrow caliber generally have valves composed of single cusps, and in the larger vessels, valves are double. Tricuspid valves in the veins are rare. Kampmeier stated that the innominate, the precava and post cava veins are valveless, but at the mouths of all their subsidiary vessels, valves are found. He found that the internal mammary vein and its branches were equipped with valves and they are so arranged that the current within the large trunk is deflected upward. The venous plexi of the vertebral column are devoid of valves, and also the spinal cord, except for the main channels which lead into the intervertebral veins.

Kampmeier found no valves in the vessels of the lungs. The openings of the hepatic veins have no valves. Splenic veins appeared to have valves capable of preventing regurgitation of blood.

In the upper limbs the veins are well endowed with valves, the deep veins having more than the superficial ones. All the branches of the femoral vein are well supplied with valves, which is true, also, of all other deep and all large superficial veins of the lower limbs.

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The final part of the document provides a summary of the key findings and conclusions of the study, and offers recommendations for further research and improvement.

MICROSCOPIC ANATOMY OF THE VEINS

1. Structure of the Veins and Venule Wall

Franklin, 1928a, describes the structure of the veins and shows that the veins vary according to calibre, age and species. Individual veins are noted to differ from one another according to their situation in the body, and the same vein is noted to vary markedly in its structure in the course of its length. Changes occur in the distribution of longitudinal and circular muscle at the level of valves. According to Epstein, 1887, the human veins have elastic fibres and muscle fibres (chiefly longitudinal) in the intima layer; mostly circular muscle-fibres in the media layer, and there is a large amount of connective tissue in the adventitial layer. There are some local peculiarities where this arrangement does not hold true.

Hooker, 1921, made a comparison between the venous and arterial blood vessels. He said that the terms "arterial" and "venous" imply a change in the character of the contained blood. The theory that the venules are found between the capillaries and veins might suggest a structural distinction, yet Hooker states that, if such a distinction is made, it must rest upon functional

THE HISTORY OF THE

REIGN OF KING CHARLES THE FIRST

By JOHN BURNET, BISHOP OF SALISBURY.

IN TWO VOLUMES.

LONDON, Printed by J. Streater, at the Black-Swan in St. Dunstons Church, in the Strand, 1680.

THE first of these two Volumes, contains the History of the Life and Reign of King CHARLES THE FIRST, from his Birth to his Execution. The second Volume, contains the History of the Interregnum, from the Death of King CHARLES THE FIRST, to the Restoration of King CHARLES THE SECOND.

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THE HISTORY OF THE

REIGN OF KING CHARLES THE SECOND

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grounds. His theory is based upon the fact that variable factors in the tissue cause an increased oxygen requirement and this increase changes the rate of the blood stream. He believes that such a change, in the rate of blood flow, will shift the point of distinction between the capillaries and venules first in one direction and again in another. Hooker stated that newer observations have shown a sharp distinction between the venules and arterioles. He explained this distinction as follows: the difference between the arteries and the arterioles is a progressive decrease in the size of the lumen and a decrease in the thickness of the muscular layer. The step down to the arteriole is performed by elimination of the connective tissue layer between the endothelial lining and the muscle fibres. The arteriole is then only composed of endothelium and a muscular layer. Subdividing of the arterioles into smaller arterioles results in a loss of the muscular layer leaving only the bare endothelial tube which makes up the capillary. Next, the capillary is transformed into a venule by addition of a connective tissue layer. Thus, we have our sharp structural contrast between the arteriole and the venule. The arteriole has muscular tissue overlying the endothelial tube while the venule has only the connective tissue overlying the endothelium.

2. TISSUES OF THE VEINS

The Endothelium

The endothelial layer of the veins is a fine, colorless, transparent structure, composed of cells very much like those of the endothelial layer in the artery, except that these cells are more oval and less fusiform. This layer makes up the inner coat of the vein.

Cunningham, 1924, stated that the importance of the endothelium in the large veins consists in its efficiency as a smooth lining, a surface which does not easily impede the passage of the bloodstream. It is also important in that there are no irregularities to cause masses of cells to adhere to its surface. He offered the idea that, since it is a living membrane, it may have an important effect upon the blood, thus accounting for some of the differences between blood in vivo and blood in vitro. Cunningham said that the endothelium plays its most important part in the smallest veins. Hooker, 1921, also mentioned the importance of the endothelial layer in the small veins. These small veins are much like capillaries in structure and are, unlike the smallest arteries, devoid of smooth muscle.

The Connective Tissue

Another important feature of the venous system is the occurrence of connective tissue sheaths around certain of the veins. Bize, 1896, found that the loose connective tissue is partly responsible for the variation in thickness of the vessel wall. The connective tissue is less in amount around the smaller veins than around the larger veins. The connective tissue is less in amount around the larger veins than around the arteries. Bize stated that the function of the connective tissue is to protect the vessel, to allow sliding, to give support to the vasa vasorum, to isolate the vessel, and to aid the valves by prevention of too great distention of the vessel. Hooker, 1921, stated that the connective tissue, as a rule, differentiates the venule from the capillary and small arteriole. The venule has a layer of connective tissue next to the endothelium, while the arteriole has a muscular layer overlying the endothelial tube. The theory is held that veins have greater internal bursting pressure than do the arteries because of a greater quantity of connective tissue in the veins. There is no definite proof for this, however.



The Elastic Tissue

The large and middle-sized veins have a considerable amount of elastic tissue. An elastic layer of fibres is found in the form of a network in the internal coat of the vein wall. The middle coat of the vein wall has elastic fibres intermixed with connective tissue. The outer coat consists, as in the arteries, of areolar tissue, with longitudinal elastic fibres. Carey, 1924, observed in bladder experiments that the veins do not have a large amount of elastic tissue, nor are they subject to a large amount of distending influence. The elastic tissue seemed to vary in amount depending upon the size of the animal. The elastic fibres were observed to run either transversely, obliquely, or longitudinally.

Franklin and Haynes, 1927, made anatomical observations on the carotid veins in a giraffe's neck. He suggested that the elastic tissue of a vein functions for the accommodation of sudden variations in volume of the vessel. These elastic elements are also necessary for the return of the vein to its original calibre after the vessel has been under a distending influence. Clarke, 1933, experimented with the elasticity of the veins by applying the formula for obtaining the coefficient of linear stretch (Young's Modulus.) She determined the elasticity of the tissue by measuring

the extension of a strip of tissue with a known weight, and then using the formula for Young's Modulus. Her resulting figures showed a wide variation of elasticity with different subjects, but there was a consistent progressive fall with age, as far as the coefficient of functional activity was concerned.

The Smooth Muscle

Cowdry, 1938, explained that the venule is only scantily supplied with muscle in the form of Rouget cells, which are supplied with constrictor nerves. He stated that the typical venule consists of an endothelial tube encased in a varying amount of collagenic and elastic tissue in which there are few fibroblasts. There is no real muscular layer. In the veins, muscle is found in rather large quantity. The media is composed chiefly of circular layers of smooth muscle though much thinner than is the smooth muscle layer in the artery.

Evans, 1926, observing the smooth muscle of the veins, found that it seemed to react as does other smooth muscle. The smooth muscle in the veins may be either longitudinal or transverse, or both, or it may be absent altogether. Bardeleben, 1877, suggested that the longitudinal muscles act on constriction as veno-dilators, and the circular muscles act as veno-constrictors.

Nonidez, 1937, studied the layers of tissue present in the superior vena cava and inferior vena cava of both the dog and the cat. He observed that, as the superior vena cava approaches the heart, it loses the musculature of the thin media and, in place, there is a coat consisting of the anastomosing striated muscle fibres characteristic of the myocardium. The transition occurs rather abruptly. This extension of the myocardium into the wall of the vein was found to be rather constant in all the animals examined. These fibres were gathered into bundles of varying sizes in a circular arrangement. In both the dog and cat, the inferior vena cava showed an extension of the myocardium similar to the myocardial investment of the superior vena cava. The pulmonary veins showed a similar investment of the myocardium, though it was thinner and less compact than in the venae cavae.

The Nervous Elements

The smooth muscle of the vein is innervated by nerves derived from the sympathetic nervous system. Hooker, 1921, in his study of the veins, found no evidence that any but the largest veins contained sensory nerve fibres. The nerve fibres, innervating the small veins, venules and capillaries, were observed to be

of such a fine structure that a motor or sensory differentiation was impossible. In the larger vessels, sensory end-plates were visible, but this was not so in those of smaller calibre. He stated that in the case of the venules, which are devoid of smooth muscle tissue, the phenomenon of contractility, if present at all, must have another basis.

Sollman, 1922, made a study of the autonomic supply of the veins. He noticed that the veins appeared to have only a single innervation, as judged by nerve stimulation. They appeared to have this single innervation because one nervous system was so predominant over the other that only one seemed to be present. Most of the vessels observed were innervated by the sympathetic nervous system responsible for constriction. In a few cases, a dilator effect was produced which, he explained, was the result of a parasympathetic innervation.

Horiuchi, 1924, also studied the nervous elements present in the walls of the veins. His efforts resulted in a large amount of evidence confirming the presence of sympathetic fibres in the vein wall. Some afferent fibres were also found, but parasympathetic fibres were not evident.

Monidez, 1941, while still working on the morphology of the veins adjoining the heart, found two kinds of nerve receptors.

The first type of a receptor was the subendothelial nerve ending which appeared flattened with its branches parallel to the endothelium. From histological studies, he concluded that these nerve endings are excited by an increase of blood pressure, thus causing a reflex cardiac acceleration (Bainbridge's reflex). The second type of receptor which he observed was a perimuscular nerve ending, found in the walls of the pulmonary veins. The presence of the receptors in the pulmonary veins indicated that they may also be responsible for Bainbridge's reflex upon a rise of blood pressure in these veins.

3. VASA VASORUM

Little, if any, recent research has been done on the tiny blood vessels which are distributed in the walls of larger veins. Epstein, 1887, found that the veins are more richly supplied with vasa vasorum than the arteries which he explained by greater desaturation of the blood in the lumen of the vein than in the artery. The vasa vasorum were found in vessels of not less than 1 mm. in diameter. The vasa were usually only in the adventitia, but, in some of the larger veins, the media also contained the capillary network.

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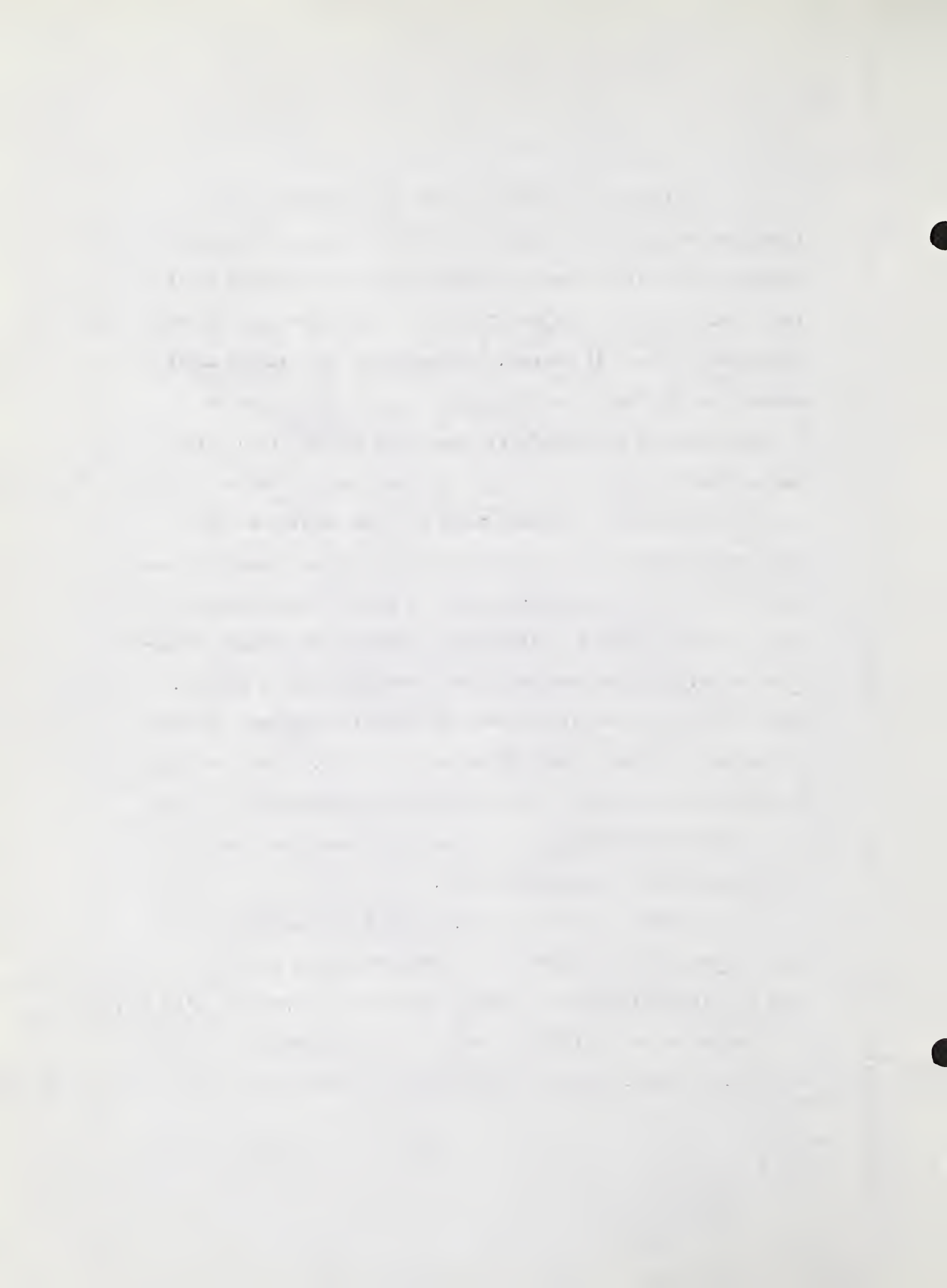
PHYSIOLOGY OF THE VEINS

A. VENOUS PRESSURE

Venous pressure was first measured in the experiments of Stephen Hale, 1904, by merely connecting an upright tube to a vein of a living animal and measuring the height to which the blood rose in the tube. Since that time new and better methods have been devised. Bedford and Wright, 1924, attempted to find the factors determining normal pressure in the peripheral veins. They concluded that there were four factors determining normal pressure. They are as follows: (1) the capillary pressure which depends indirectly on the arterial pressure and is regulated by the arterioles and capillaries, (2) the negative intra-auricular pressure which consists of a suction action due to the negative intra-thoracic pressure maintained by the recoil of the lung, (3) the hydrostatic relationship of the vein to the heart, and (4) the volume of the blood in the veins. Bedford and Wright stated that, since the veins are so distensible, they can accommodate increased volumes of blood without a very large increase in the internal pressure in the vein.

Eyster, 1926, studied the clinical applications of venous pressure. He found that the pressure of the blood in the vascular system is uniform throughout as long as the heart is at rest. Measurement of the mean "hydrostatic pressure" in the dog showed about 10 mm. of mercury. He explained that, as the heart beats, blood is forced into the arteries and a difference in pressure develops as a result of resistance to the flow of the blood. This resistance to the flow of the blood is greatest in the smallest vessels. The resistance has come to be known as "peripheral resistance." In further studies on the venous pressure, Eyster and Meek, 1930, observed that the venous pressure in dogs under anesthesia showed little change, although the physical conditions existing in the cardiovascular system are greatly altered. They could find no relation between the arterial pressure and the pressures in different parts of the venous system. Eyster and Meek found that an inconsistent venous pressure was dependent upon the differing responses of the heart to varying venous loads and a variable capacity of the vascular bed.

According to Landis, 1933, calculations and direct observations proved that arteriolar capillary pressure is higher than venous capillary pressure. In the frog, Landis observed an arteriolar capillary pressure of 14 cm. of water and a venous capillary pressure of 10 cm. of water. In man, the arterial capillary pressure was



45 cm. of water and the venous capillary pressure was 22 cm. of water. A comparison was made of the osmotic pressure of the plasma colloids to the venous and arteriolar capillary pressure. The average venous capillary pressure was below the osmotic pressure of the plasma, but the average arteriolar capillary pressure was above that of the osmotic pressure of the plasma. Landis offered the suggestion that fluid is filtered from the blood while passing through the arteriolar part of the capillary and absorption takes place in the venous part of the capillary network.

1. MEASUREMENT OF VENOUS PRESSURE

Indirect Method

The indirect method for the determination of venous pressure was the first method used to any extent. Frey, 1902, was first to use this method in which pressure is applied over a superficial vein and the amount, required to produce collapse of the vein, is determined. Frey made use of a pelotte to which he attached weights until collapse was accomplished. Gaertner, 1903, devised a method which consisted of determining the level at which a superficial vein of the hand goes from a state of filling to a state of collapse. He found that the collapse of the vein occurs at the level where the negative hydrostatic pressure is equal to

the positive venous pressure. By comparison with the level of the right auricle, one can express the venous pressure in terms of millimeters of water.

In 1904, v. Basch devised a method of measuring venous pressure, whereby he placed a glass chamber on the skin over the vein and connected to it a water manometer and pump. Air was forced in until the vein was noticed to have collapsed. He obtained a pressure averaging about 10.7 mm. of mercury in the superficial hand veins. A method was used by Frank and Reh, 1912, whereby two sphygmomanometer arm bands were placed around the arm, one around the upper arm, the other around the forearm. By inflating the lower cuff, which was connected to a tambour writing on a smoked drum, it was possible to make a record of vibrations in volume in the forearm. The upper cuff was attached to a water manometer and was inflated until the volume of the forearm began to increase. This indicated a change in the venous flow. The recorded pressure here was taken as the mean venous pressure of the superficial veins of the forearm. They obtained values ranging from 10 to 60 mm. of water.

A new indirect method for determination of venous pressure was devised by Sweeney and Mayerson, 1936. They used a rubber-celluloid capsule which was placed directly over the vein to be measured. Use of the celluloid capsule had a number of

advantages over the other devices used to produce collapse of the vein. This type of capsule provided an air-tight skin contact; there was a small amount of skin distortion; and there was no need for lighting for good visibility. Readings made with the celluloid capsule have been checked with recordings made by other methods and a high degree of correlation was found.

Direct Method

The direct method of measurement of venous blood pressure requires that a cannula be inserted into the vessel and retained there long enough to obtain complete balance between the blood in the vessel and the fluid in the manometer. Moritz and V. Tabora, 1910, were the first to use this method. They obtained figures ranging from ten to ninety millimeters of water (0.8 to 7 mm. of mercury) in the median vein. According to Eyster, 1926a, the direct method for determination of venous pressure by inserting a cannula (trocar) directly into the vein and connecting it with a manometer, gave a fairly accurate figure. A comparison was made with figures obtained by the capsule pressure method (indirect) and a very close correspondence was found. He found that several of the determinations made by the direct method were somewhat higher than those obtained by other workers with the indirect method. Eyster attributed the higher figure obtained by the

direct method to the influence of venous pressure in the arm from the partial or complete occlusion of the larger vein draining the peripheral bed. In the direct method, the vein collapses under pressure, produces stagnation of venous flow, and thus, may produce an abnormally high reading. Of all the indirect methods, probably only the method used by Frank and Reh, 1912, (the use of two sphygmomanometer arm bands) would be subject to the same criticism, because of such widespread venous obstruction. Eyster, 1926, stated that the indirect method had an advantage over the direct method in that many readings can be made of a patient without much difficulty. Kloff, 1939, by the use of a new method, (a needle irrigated with sterile citrate solution to prevent the clotting of the blood which always enters the needle to some extent) found normal values to range from 30 to 90 mm. of water.

Burch and Sodeman, 1939, pointed out the influence of tissue pressure upon the recordings made of venous pressure. They explained that there is a positive pressure in the tissue spaces which is exerted upon all the contained structures, including the blood vessels. This tissue pressure was found to oppose the intravascular pressure. By subtracting the tissue pressure from the intravascular pressure, a fairly accurate estimate of venous pressure was obtained.

A new method for measurement of venous pressure was devised by Burch and Windsor, 1943. They realized that venous pressure measurements had been neglected because the apparatus was difficult to use, as well as too bulky to carry. A new instrument, called the phlebomanometer, was constructed. This apparatus was based upon the principles of the aneroid manometer for recording arterial blood pressure, but far more sensitive. This new instrument made it possible to measure the pressure in the small veins.

2. RELATION OF VENOUS PRESSURE TO PERIPHERAL VASCULAR BED

Bayliss and Starling, 1894, were among the first to observe the relation of the peripheral vascular bed to venous pressure. They found that by removal of vasoconstrictor control (by the cutting of splanchnic nerves) there was a fall in the arterial pressure, but that there was no change in venous pressure. Bayliss and Starling explained that the peripheral vascular bed increased in volume instead of affecting the pressure in the veins. Since the work of Bayliss and Starling, there has been evidence presented to show the independence of venous pressure to peripheral resistance. Nolf and Plumier, 1904, could find no effect on the venous pressure in the systemic veins during a period of asphyxiation where there was vasoconstriction, until the heart began to fail. Eyster and Middleton, 1924, demonstrated the ability of the circulatory bed to adapt itself to prevailing conditions and to maintain a constant venous pressure following changes in blood volume in dog and in man. No change in the venous pressure resulted, though a change in vascular tonus was produced by warming or cooling the hands. White, 1924, confirmed these findings.

3. THE RELATION OF VENOUS PRESSURE TO CARDIAC OUTPUT

While Patterson and Starling, 1914, were working on the circulation of a heart-lung preparation, they found a direct relation between venous pressure and the diastolic filling and the systolic discharge up to a maximum venous pressure of 250 mm. of water. This work has been criticized because of the absence of the pericardium which exerts a resisting influence. Patterson and Starling stated that the systolic output is a linear function of venous pressure. Wiggers and Katz, 1922, in their studies, found a variable systolic discharge as the venous pressure was increased, up to just short of signs of cardiac decomposition, 250-310 mm. of water. Henderson, 1923, found that a normal range of venous pressure produced no change in the stroke volume of the heart. This is known as the law of Uniformity of Cardiac Behavior. In 1925, Henderson and Haggard revised the former findings of Henderson concerning the resting stroke volume and its change during activity. The normal stroke volume was observed to be between 1.3 and 1.8 ml. per kilo of body weight during slight activity, but during rigorous exercise it rose to 3.5 ml. This might seem to confirm the belief that there is a variable stroke volume depending upon the venous

THE HISTORY OF THE UNITED STATES OF AMERICA

The history of the United States of America is a story of growth and change. It begins with the first settlers, who came to the continent in search of a new home. They found a land of vast resources and opportunities, but also one of many challenges. The early years were marked by conflict and struggle, as the settlers fought to establish their communities and defend their rights. Over time, the United States grew in size and power, becoming a major force in the world. The country has faced many challenges, including wars, economic crises, and social movements. But through it all, the United States has remained a land of hope and opportunity, a place where people can live free and pursue their dreams.

return. Eyster, 1926b, stated that a reduction in cardiac output would tend to produce stagnation in the venae cavae and result in a rise of venous pressure. Likewise, increased cardiac output would tend to cause a depletion of the veins and result in lowering of the venous pressure. From this observation, he stated that cardiac output is the variable, and the changes in venous pressure the result. In recent years, however, venous pressure has come to be considered as the main factor in determining cardiac activity. The concensus of opinion seemed to be that venous pressure and cardiac output are interdependent, and that cardiac activity is an important factor in the stabilization of venous pressure at a fair level.

4. THE EFFECT OF TEMPERATURE ON VENOUS CIRCULATION

The effect of local temperature upon the peripheral circulation was studied by Goldschmidt and Light, 1925. When the hand was immersed in water below 18 degrees, the skin showed a condition of hyperemia; the oxygen content of the blood increased, while the carbon dioxide content in the blood decreased. It is explained that the arterioles and veins are partially constricted while the vessels, which give color to the skin are dilated. Goldschmidt and Light believed that constriction of the veins causes a heightened pressure in the capillaries and venules, thus, a partial dilation. When the hand was placed in water of 18 to 39 degrees centigrade, it assumed a pale or bluish color. This was due to increased oxygen unsaturation of the capillary blood. (A blue color produced by the cold is due to vaso-constriction and a decreased blood flow.) The hand was placed in water of temperatures of 40 to 60 degrees centigrade producing a reddish or purplish color of the skin. Evidence shows that there is a dilatation of the whole vascular bed. Goldschmidt and Light summarize their work by stating that the skin and subcutaneous tissue tends to assume the temperature of the surrounding medium.

Sribyatta and Bazett, 1928, studied the effect of local changes in temperature upon the blood from the veins in the hand, and found that for each degree fall of temperature the pH of the blood increased by 0.014 and the pOH value increased by 0.018.

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5. THE EFFECT OF MUSCULAR ACTIVITY ON VENOUS PRESSURE

White, 1924, performed extensive research on the effect of muscular activity on venous pressure and found that in light muscular work on a stationary bicycle an elevation of venous pressure amounting to 40 to 50 mm. of water, falling immediately to normal upon cessation of activity. During laborious work, the venous pressure rose very high. Bedford and Wright, 1924, found a venous pressure of 95 to 195 mm. of water immediately after rigorous exercise which fell rapidly to normal during rest periods. In the experiments of Proger and Dexter, 1934, moderate exercise involving the lower extremities produced no change in the blood pressure of the veins of the upper extremities. Upon observing the superficial and deep veins of the upper extremities, the velocity of the blood flow was rapid when the arm was hanging down, but slower when the arm was held in an erect position. Schneider and Collins, 1938, found that venous pressure rises and remains up during work on the bicycle ergometer. When the load of work is too heavy, the venous pressure rises steadily until fatigue takes place. After physical exertion, the venous pressure ordinarily returns to normal. The time required for this depends upon the extent of the physical exertion. After conditions of rigorous exercise, it required as much as 22 to 27 minutes to return to normal.

6. THE EFFECT OF BED REST ON VENOUS PRESSURE

Hooker, 1914, found a rise of venous pressure during the walking hours and during sleep there was a gradual fall. His own venous pressure was 100mm. of water before arising in the morning and by the time for retiring it had risen to 200 mm. of water. Eyster and Middleton, 1924a, made extensive observations on hospital patients in bed for minor surgical conditions. All the venous pressure readings were relatively low with the usual readings close to 50 to 60 mm. of water. The venous pressure average of those sitting up or walking about was, on the average, much higher. They observed that bed rest conditions in the prone position caused the venous pressure to become stabilized within a narrowed margin.

7. THE EFFECT OF POSTURE ON VENOUS PRESSURE

Many physiologists have studied the effects of posture upon venous pressure. Thus, it would be impossible to list the results obtained by each one. Eyster, 1930, observed that the venous pressure, with the body in the recumbent posture, averages between 40 and 60 mm. of water. In cases where the heart began to fail, the venous pressure rose to as high as 200 mm. of water or even higher. Determinations of venous pressure were made in a

ORIGINAL ARTICLES

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2. The Effect of the Diet on the Course of the Disease in the Case of the Patient with Diabetes Mellitus
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series of normal, healthy young women of college age, by McIntire and Turner, 1934. The venous pressure was determined in the superficial veins of the hands and, contrary to the findings of others, there was constancy of pressure, in spite of changes of posture. Mayerson, 1942, found that when subjects were placed in an erect position, there was a marked retardation of blood flow in the lower extremities. This appeared to be due to a stagnation or pooling of blood in the veins. Goldbloom, Kramer, and Lieberman, 1940, revealed that when a normal man stands, the tendency of gravity to decrease the venous return to the heart is offset by compensatory mechanisms so that no significant fall in cardiac output results.

8. THE EFFECT OF AGE ON VENOUS PRESSURE

Venous pressure measured in the veins of the arm or hand by Hooker, 1914b, was found usually between 100 and 200 mm. of water and increased progressively with age from 80 mm. in early youth to 250 mm. in old age. Hooker, 1916, in further study of age groups between 5 and 85 years, proved that there was a rise in pressure with increasing age. His readings were made in the sitting position. Eyster and Middleton, 1924a, in their work, could find no relationship between age and venous pressure. Gibson and Evans, 1937, observed no significant variations in either blood pressure or blood viscosity rate with age in either sex. Recent research explains Hooker's findings were influenced by postural factors.

1875
The following is a list of the names of the persons who have been elected to the office of Justice of the Peace for the year 1875. The names are given in alphabetical order of their surnames. The names of the persons who have been elected to the office of Justice of the Peace for the year 1875 are as follows: [illegible text]

[illegible text]

9. THE EFFECT OF GRAVITY ON VENOUS PRESSURE

Some of the early investigations done on the effects of gravity upon venous pressure were performed by Hill, 1895. He showed that, if the tonus of the peripheral vessels was destroyed, the vascular bed became engorged with blood and death resulted from decreased return of venous blood to the heart. The tonus of the vessels supplied with splanchnic nerves was developed to the highest degree in upright animals (monkey, and man.) Venous pressure was found to rise in the veins of the hand held at different levels below the heart until high enough to overcome the hydrostatic pressure and thus, cause a return of venous blood. Sewall, 1906, observed a rise in pressure in a vein of an arm when the other arm was elevated above the head. This, he believed due to the hydrostatic emptying of the veins into the vena cava. Eyster, 1926c, emphasized the importance of the hydrostatic factor in the determination of venous pressure. The hydrostatic factor was found to amount to approximately 0.76 mm. of mercury pressure for each cm. of venous pressure. Holt, 1940, eliminated the hydrostatic factor in the measurement of the brachial venous pressure by measuring the subject first in the supine position and then in the prone position. Venous pressure was found to be equal to one half of the sum of the two pressures.

10. THE EFFECT OF RESPIRATION ON VENOUS PRESSURE

The relation of venous pressure to the phases of respiration in man have been studied by many investigators, but there is no definite agreement. According to many workers, the venous pressure falls in the experimental animal during inspiration and rises during expiration. Fuchs, 1921, observed a falling venous pressure in the experimental animal's arm vein with inspiration while the opposite relation was held in the leg. Respiratory variations amounted to as much as 30 mm. of water in a few cases. Kroetz, 1922, noticed respiratory variations in pressure in the peripheral veins of man, usually 0.5 to 2 mm. of water and often 4 mm. of water. He did not relate the fall of venous pressure to the phase of respiration. Waud, 1924, used an indirect method of measurement of venous pressure and found a pressure rise during expiration which continued into the phase of inspiration. Runge, 1924, found a slight fall in venous pressure in inspiration in about one-third of the cases studied. The fall in pressure was seldom more than 10 mm. of water. His observations were made by direct cannulation of the vein.

Harrison, Harrison, and Marsh, 1932, advanced an hypothesis that there might be a reflex effect on respiration

similar to Bainbridge's reflex acceleration of the heart. They performed experiments on a number of dogs, first by injecting a fluid, (saline, Ringer's, or defibrinated blood) into the external jugular vein or inferior vena cava. There was a marked increase in the respiratory rate when the vagus nerves were intact. After bilateral vagotomy, there was only a slight increase in respiration noted when the fluid was injected. In a second experiment air was injected by the use of a balloon attached to a condom which was passed into the right auricle by way of the vena cava. Twenty cm. of air caused a progressive increase in respiratory rate. A deflation of the balloon caused a reversed change. He summarized his findings by stating that an increased venous pressure is accompanied by increased respiratory rate in the ventilation of dogs with intact vagi. There was usually no effect after double vagotomy.

11. THE EFFECT OF VENOUS TONE UPON VENOUS PRESSURE

Evidence has been supplied by various investigators to prove that venous pressure is partially dependent upon the tone of the containing vessel. Two early investigators, Roy and Brown, 1897, found a variable tonus in the individual capillaries and venules which was responsible for alterations in the vascular bed.

Adriani and Rovensteine, 1940, found that a disappearance of venous tone following high spinal anesthesia is indicated by the sudden decrease of venous pressure. Schiappoli, 1940, attributed the changes in venous pressure following thermal and mechanical stimuli applications to the carotid sinus to changes in venous tone. Schiappoli, however, was unable to produce consistent changes by increasing carotid sinus pressure. He considered venous tone as the determining factor influencing venous pressure.

12. VENOUS PRESSURE FACTORS IN CIRCULATORY FAILURE

Harrison, 1938, in his studies of circulatory failure, found that a decline in blood volume tended to produce a lowering of the venous pressure. The veins appeared to collapse and made cannula insertion difficult. Harrison observed that the amount of blood which was expelled from the heart during systole depended upon the amount that entered during diastole and this was, in turn, dependent upon the venous pressure. In a condition of right-sided heart failure there was a heightened venous pressure which caused an accumulation of fluid in the body tissues. Blalock and Harrison, 1927, observed that the cardiac output was diminished in conditions which caused a low venous pressure during a condition of hemorrhage. In various types of shock the cardiac output is also diminished and a low venous pressure results as observed by Blalock, 1933.

Harrison, Jr., 1934, revealed that the cerebrospinal fluid pressure bears a close relationship to the venous pressure in patients with congestive heart failure. Harrison, 1938, observed that failure of the left side of the heart had no effect on systemic venous pressure until failure of the right side of the heart developed.

B. NERVOUS CONTROL OF THE VEINS

The nervous control of the veins is not so well understood as is the control of the heart or arteries. There are two influences which affect the blood vessels, the vasoconstrictor and the vasodilator mechanisms which are considered partly nervous and partly chemical. The occurrence of constriction or dilatation in the veins has received little attention. McDowall, 1935, stated that these impulses come from the central nervous system, especially from the medulla where the vasoconstrictor and vasodilator centers have been found. The sympathetic nervous system was believed to be responsible for constriction of the veins of the skin and the intestine and, as a rule, dilatation of the veins of the muscles and the heart. The parasympathetic nervous system was usually responsible for dilator action.



Donegan, 1921, observed that the portal vein was closely accompanied along its course by a nerve. It appeared to him that there might be a possibility that the current of the nerve stimulated the muscle fibres of the vein. He performed an experiment whereby he removed the connective tissue sheath of the vein. The nerve to this denervated vein was stimulated and he found that the denervated portion remained inactive while the rest of the vein constricted. Bayliss and Starling, 1894a, also showed that branches of the portal vein could be caused to constrict. They found that the venoconstrictors leave the spinal cord in the nerve roots from the third to the eleventh thoracic vertebrae, especially in the fifth to the ninth.

Bancroft, 1898, made an investigation of the venoconstrictor nerves to the veins of the hind limbs of a dog. The nerves were observed to leave the cord in the first to fourth lumbar segments and go by way of the rami of the sixth and seventh lumbar and the first and second sacral to join the sciatics. Donegan, 1921a, investigated the venoconstrictors nerves of the dog, cat, and the rabbit. He found that the superficial veins of the hind limb of a cat and dog receive sympathetic fibres which originate in the second, third, and fourth lumbar roots, chiefly by way of the seventh lumbar and first sacral ganglia. The veins of the fore-limb received nerve fibres from the sixth to eighth

thoracic segments. The cell-stations were mainly in the stellate ganglia. Horiuchi, 1924, found the cutaneous veins of the hind limbs of dogs supplied with antidromic vasodilator mechanisms from the posterior roots of the seventh lumbar, and first and second sacral segments. Reflex dilatation was effected by inhibition of the constrictors or by stimulation of the dilators.

Donegan, 1921, also studied the mesenteric veins. In his experiments constrictions resulted from the stimulation of the nerves from the inferior mesenteric ganglion. He found that the mesenteric veins were supplied with sympathetic nerves having their cell-stations in the ganglia of the solar plexus and the inferior mesenteric ganglia. The mesenteric veins were influenced reflexly in the same way as the arterioles. Hooker, 1918, also obtained evidence of constriction of mesenteric veins on stimulation of nerve fibres from inferior mesenteric ganglia. Horiuchi, 1924a, found that the inferior mesenteric vein in the same way received dilator fibres from the posterior roots of the twelfth and thirteenth thoracic segments.

Studies which were made of the veins from the muscles and vena cava showed no effect to nerve stimulation in the work of Donegan.

Henderson, 1943, suggested a new type of nervous control over the circulation, as demonstrated in the venopressor mechanism. He made a distinction between the vasomotor reactions and the venopressor reactions. The vasomotor reactions are those concerned with the adjustment of arterial pressure and distribution of blood. The venopressor reactions are mainly concerned with the adjustment of the volume of the venous return, and thus, with the minute volume of the circulation. He stated that, since nearly every action in the animal body has an influence upon all processes, it is possible that there is no vasomotor adjustment without an accompanying venopressor reaction. Henderson believed that the venopressor mechanism explained the problem of circulation during a condition of shock. An examination of the veins in the splanchnic area, during a state of shock, revealed that the veins were not over filled nor congested, contrary to the original conception. He explained that, during shock, the blood need go nowhere but remain where it was before the failure. (Since the venopressor mechanism no longer pushes the blood forward, the veins collapse and the asphyxial tissues absorb the serum.)

C. THE ACTION OF DRUGS ON THE VEINS

The study of the effect of drugs upon the blood vessels has been largely confined to the effect of drugs upon the arteries and the arterioles. Few investigators have dealt with the

veins, and those few have been largely concerned with the effects of adrenalin upon them.

1. EPINEPHRINE (Adrenalin)

The suprarenal glands of all vertebrates contain a substance, epinephrin (adrenalin), which is a powerful stimulant, and is normally discharged into the blood vessels. The effects of epinephrin are for the most part identical with those of stimulation of the sympathetic nerves. Edmunds and Gunn, 1936, stated that epinephrin introduced its effect by stimulating the mechanism lying between the nerve and the muscle. They explain that the drug does not act directly upon the contractile muscle, because some involuntary muscle contracts while other involuntary muscle relaxes. The drug does not act directly upon the nerve ends, for after these have degenerated and disappeared, the usual effects can be obtained by injection of the adrenalin. Edmund and Gunn, 1936, stated that the action takes place upon a substance, called the "receptive substance," which is between the nerve and the contractile material.

The early researchers dealing with the effect of drugs upon the veins were Gunn and Chavasse, 1913. They found that circular strips of sheep's external jugular and mesenteric veins strongly contracted with adrenalin, 1 in 100,000, while the vena cava contracted less markedly.

Hartman, Evans, and Walker, 1928, experimented with the action of epinephrin by injecting the drug into the jugular vein. Adrenalin ranging from 0.2 cc. of 1:100,000 to 1 cc. of 1:10,000 was used. A dilatation of the veins and venules was produced as well as dilatation of the arteries, arterioles, and capillaries. With a larger dose, 1 cc. of 1:100,000, constriction of the veins and arterioles resulted and the capillaries were thought to have dilated.

Daly, Foggie, and Hebb, 1940, studied the action of adrenalin on the pulmonary vascular bed. Experiments on lungs which were perfused in the normal and reverse direction with injections of adrenalin into the bronchial arteries, produced a constriction of both the arteries and veins.

Connet, 1920, performed an extensive series of experiments upon both dogs and cats to determine the effect of adrenalin upon venous pressure. With doses of 0.15 mgm., small increase in venous pressure was produced whether the heart rate was increased or decreased. She believed that adrenalin had only a small effect upon venous pressure. Hoskins, 1922, found that venous pressure was little affected by adrenalin (except in large doses which resulted in a back pressure from the heart).

Watkins, Weiss, and Haynes, 1938, experimenting with the effect of epinephrine on circulatory collapse, induced by sodium

nitrite, found that epinephrin injected into the hand in subcutaneous doses of 10. mgm. caused an increased venous tone and a slightly elevated venous pressure as well as arteriolar constriction and reduced blood flow.

2. CHOLINE

The effect of acetylcholine upon the veins has not received the attention of many investigators. Feldberg, 1933, demonstrated that, following lingual nerve stimulation, an acetylcholine-like substance appeared in the venous blood flowing from the tongue. An intravenous dose of eserine previous to the experiment is necessary to inhibit its otherwise rapid destruction. The similarity of the substance produced to acetylcholine was established in several different ways. Snyder and Tyler, 1941, demonstrated the action of acetylcholine upon the vessels of the liver. A constriction of the hepatic venules was produced in a peristaltic-like manner. The hepatic outflow was increased temporarily and the resistance to the inflow was raised. Following this, there was a dilation of the sinusoids and portal veins and an increase in liver volume. Upon the release of the hepatic venous resistance, the accumulated blood gushed out at a rate determined by the dosage of the drug.

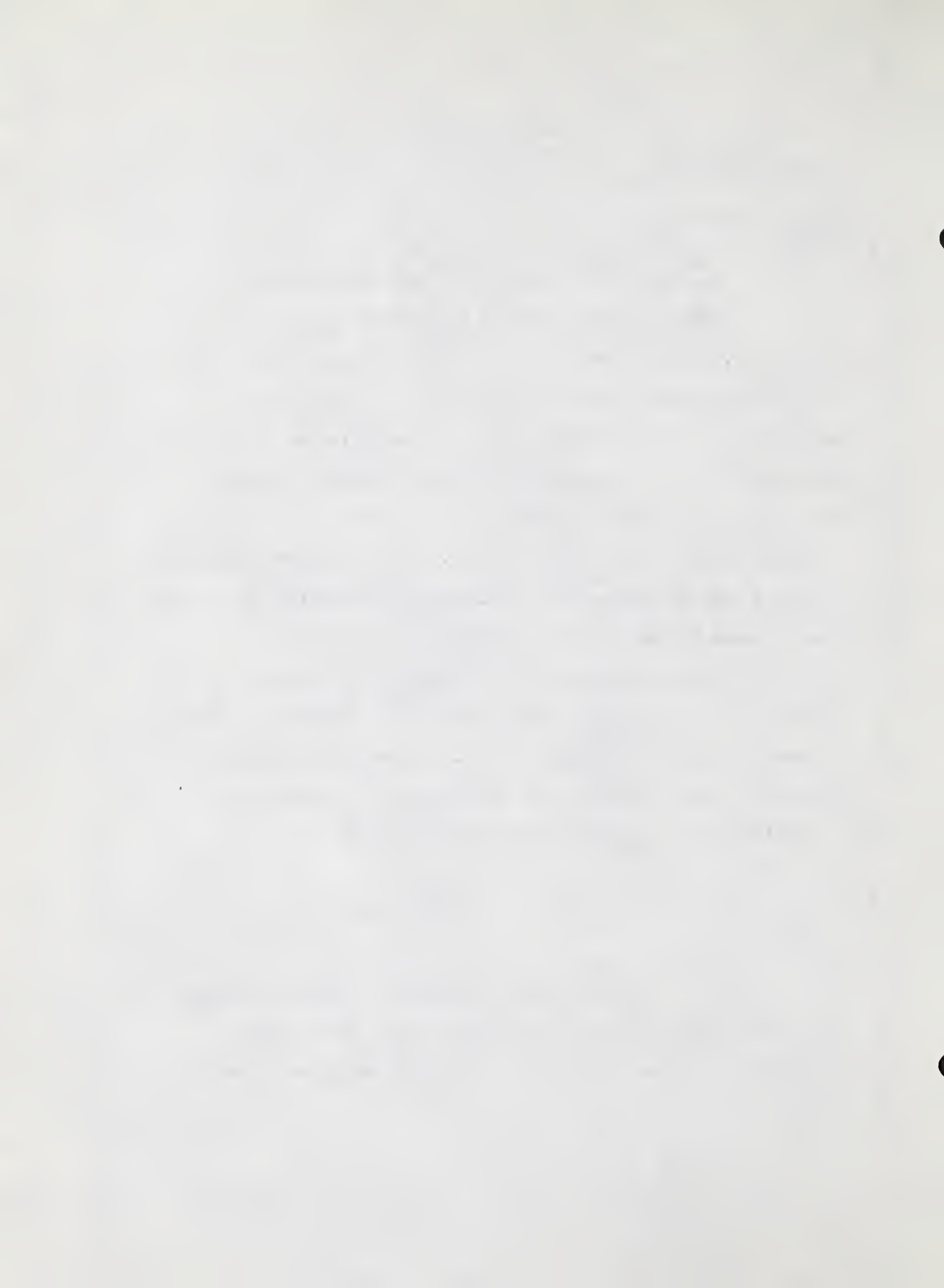


3. HISTAMINE

McDowall, 1923, demonstrated that small doses of histamine produced a rise in venous pressure in cats under light anesthesia. When the degree of anesthesia was increased, no effect of the histamine was noticed. Dale, 1929, and Feldberg, Schilf, and Zernik, 1928, found only little or no constriction at all of the hepatic vein of a cat after histamine injection. Best and McHenry, 1931, stated that the effect of histamine upon the hepatic veins is largely restricted to the dog. They stated that there is a marked similarity between the role played by the liver in anaphylactic shock and the effect of histamine upon the veins of the liver. A variation in the action of histamine on the liver in different species was attributed partly to the different amounts of smooth muscle in the hepatic veins. In the dog the hepatic veins are equipped with a stout covering of smooth muscle which was believed to be partly sensitive to histamine.

D. PERMEABILITY OF THE VEINS

Landis, 1927, in his early studies of diffusion through the walls of the small blood vessels, observed that venous capillaries, and venules were far more permeable to vital red HR



(Trypan Red) than were the arterial capillaries and arterioles. His experiments were carried out on the mesenteric vessels of a frog. Rous, Gilding, and Smith, 1930, confirmed the findings of Landis. Poorly diffusible dyes were used to prevent any possible diffusion in one part of a vessel before it had had time to reach the other extremity of the vessel. At first, the dye failed to appear outside the arteriolar part of the capillary network, but was very distinct outside the venous portion where it increased continually. They state that capillary pressure and fluid movement could not have been a factor in the greater diffusibility of the venous portion, for the blood pressure is lower here than in the arteriolar portion of the vessel. Rous and his co-workers advanced the hypothesis that the endothelium of the capillaries, serving certain organs, is relatively impermeable near the arterioles and becomes increasingly permeable as the venules and veins are approached.

Landis and Gibbon, 1933, elevated the venous pressure in the forearm whereupon he observed that the filtration was also increased. This filtration was found to be directly proportional to the increase in venous pressure in the cases which they tested. Drury and Jones, 1927, also, measured the rate of filtration in the veins and they, too, found that the rate of filtration was roughly proportional to the increase in venous pressure.

Since the small veins and venules are so permeable to water, whole blood and dyes, Swindle, 1935, advanced a theory by way of explanation. He said that we must assume the presence of small openings or fenestrae (perivascular seep valves) in the walls of the small veins. When the vessel is constricted, the fenestrae are only potential openings and the walls are very impermeable. The fenestrae become larger and the walls become permeable as the vessel dilates.

E. BLOOD MOVEMENT IN THE VEINS

1. FACTORS AFFECTING VENOUS RETURN

Present knowledge of venous return is far from complete. Henderson, 1943a, made one of the most recent studies on venous return emphasizing the importance of tonus. He held that contraction of the forearm muscles forces the blood from these muscles into the vein and on toward the heart. Rhythmic relaxation and contraction of the muscles were believed to fill the arteries with blood, which is, in turn, emptied into the veins. This, he stated, is a booster effect which aids the venous return of the blood. Krogh, 1929, found that the blood was forced out of the vein, by compression from the surrounding muscle which was followed by a relaxation and a filling with blood from the



capillary network. He believed that the muscle surrounding the vein provided an effective pump working in conjunction with the valves in the vein. This method of blood movement suggests the existence of a venopressor mechanism. Henderson, 1943, stated that there is sufficient evidence to prove that the blood could not return to the heart without peripheral aid. Shock was thought to be the result of the failure of the venopressor mechanism. Sherrington, 1906, believed that a venopressor mechanism would function properly as long as the motor centers of the spinal cord were sending out impulses to the skeletal muscle.

2. OBSTRUCTION AND STASIS

Landis, Jones, Angevine, and Erb, 1932a, observed that in human subjects with a very high venous pressure (80 mm. of mercury), considerable protein passed through the walls of the capillaries. At a low venous pressure, the capillaries were relatively impermeable to protein. Waterfield, 1931, believed that globulin was held back and that the albumin of the blood leaked through the capillary walls during venous congestion. Krogh, Landis, and Turner, 1932, were unable to associate the change of venous pressure with any leakage of proteins through the capillary wall. Landis, Honas, Angevine, and Erb, 1932b, however, did find a small amount of plasma protein in edema fluids which were produced during local venous congestion. At a venous pressure of 60 mm. of

mercury, they found an average of 0.03 per cent protein in the fluid, approximately 95 per cent of the blood protein was therefore retained.

Perlow, Killian, Katz, and Asher, 1941, observed shock following venous occlusion of a hind limb of a dog which culminated in death of the animal. This venous occlusion resulted in a loss of fluid into the leg. Plasma passed through the capillary wall first, and later whole blood passed through. These investigators supported the view that the primary factor in shock is the local loss of fluid from the blood.

White, Field, and Drinker, 1933, showed that venous congestion increased the flow of lymph as well as increased the pressure in the veins.

Krogh, 1929, found that stasis begins first in the venous capillaries and columns of packed cells (erythrocytes) are formed until the arterial side is reached. The entire capillary network, including the arterioles is said to be involved. Landis, 1927a, confirmed the findings of Krogh. Landis found that a condition of stasis begins by a concentration of corpuscles in the venous capillaries and venules. A capillary blood pressure rise is attributed to blockage of the venous capillaries by abnormally viscous concentrated blood.

S U M M A R Y

Our present knowledge of the physiology of the veins is far from complete. Many investigators have studied circulation in the mammal, but the emphasis has been placed on the function of the arterial system. The principles established so far, concerning the veins, are as follows:

- (1) Small, superficial blood vessels, which have been cut away, are capable of regenerating by sending out of endothelial sprouts from preëxisting, functional vessels which anastomose with neighboring sprouts to form a network. This network of vessels differentiates into arterioles, capillaries and venules.
- (2) Many of the veins are supplied with valves which are semilunar folds of the internal coat of the veins. Valves are more numerous in the vessels where reflux is likely to occur, thus the veins of extremities of the body are more abundantly supplied with these mechanisms which aid the blood return to the heart. The viscera, in the region of the thorax, have veins devoid of valves.
- (3) The wall of the vein is composed of three layers of tissue;

THEORY

The first part of the theory is the definition of the function $f(x)$ and the function $g(x)$. The function $f(x)$ is defined as the function which is continuous at x and the function $g(x)$ is defined as the function which is discontinuous at x .

The second part of the theory is the definition of the function $h(x)$ and the function $k(x)$. The function $h(x)$ is defined as the function which is continuous at x and the function $k(x)$ is defined as the function which is discontinuous at x .

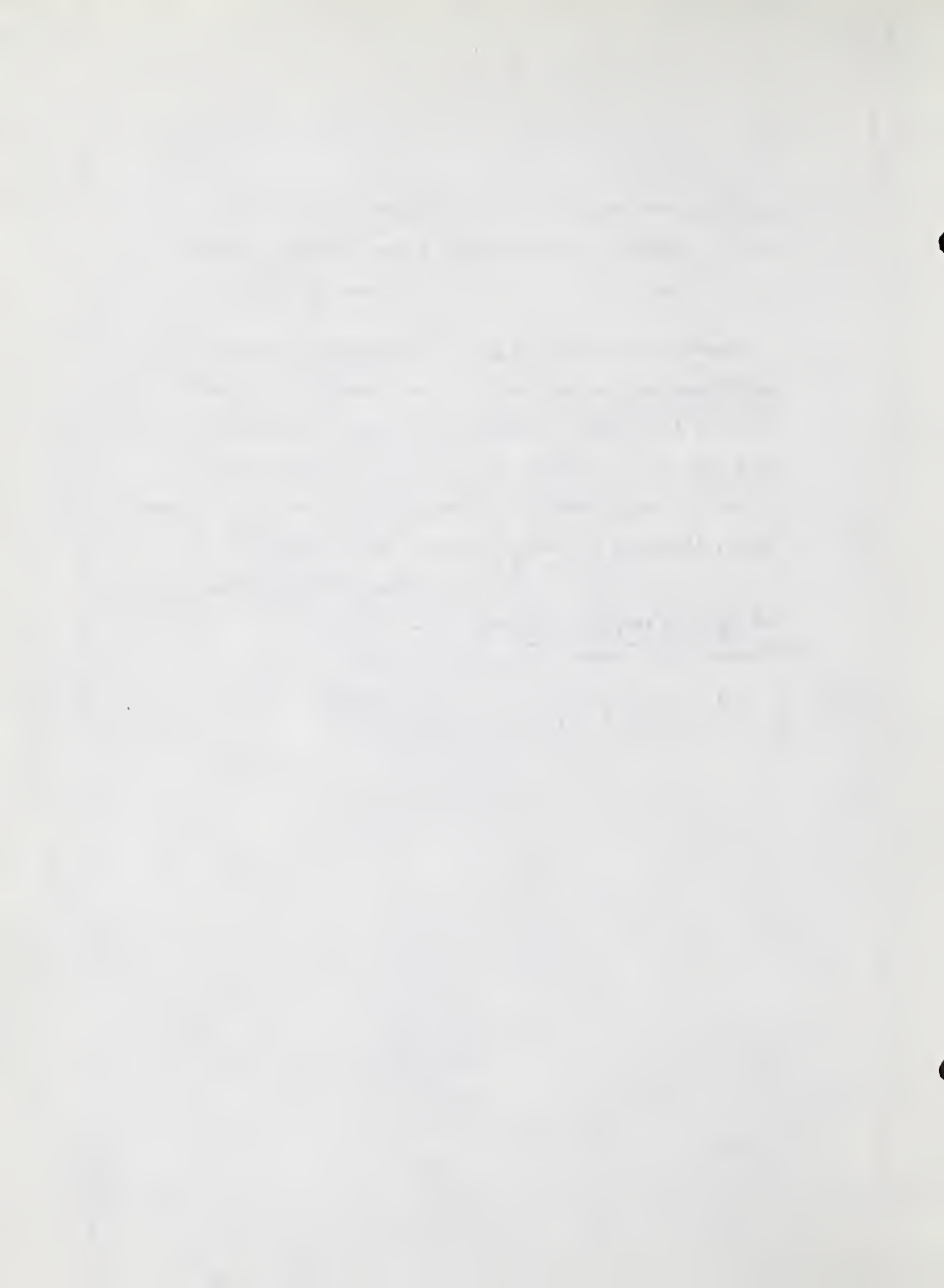
The third part of the theory is the definition of the function $l(x)$ and the function $m(x)$. The function $l(x)$ is defined as the function which is continuous at x and the function $m(x)$ is defined as the function which is discontinuous at x .

The fourth part of the theory is the definition of the function $n(x)$ and the function $o(x)$. The function $n(x)$ is defined as the function which is continuous at x and the function $o(x)$ is defined as the function which is discontinuous at x .

The fifth part of the theory is the definition of the function $p(x)$ and the function $q(x)$. The function $p(x)$ is defined as the function which is continuous at x and the function $q(x)$ is defined as the function which is discontinuous at x .

- (a) an inner endothelial lining, (b) a middle muscular layer, and (c) an external layer of connective tissue. The layers vary in the degree of development, dependent upon the size of the vein. Small veins and venules have practically no muscular layer between the endothelial tube and the connective tissue, whereas, the large veins have a thick muscular layer.
- (4) Venous pressure can be measured by direct and indirect methods producing results with a high degree of correlation. In man the normal venous pressure varies from 30 to 90 mm. of water. Venous pressure rises with increased muscular activity, increased temperature, the assuming of an erect position, and an increase in age.
- (5) The veins with a smooth muscle layer of tissue are innervated with nerves derived from the autonomic nervous system. These nerves are called vasomotor and are divided into two sets: (a) vasoconstrictor, and (b) vasodilator. The vasomotor nerves are connected with the medulla oblongata, which constantly sends out impulses to the vessels, thus keeping them in a state of tonus.
- (6) Adrenalin (Parke Davis) constricts only the veins which have a smooth muscle tissue layer. Venules rarely constrict. Histamine constricts only those veins with a stout covering of smooth muscle. Choline gives inconsistent results.

- (7) The veins and venules are more permeable than the arteries and the arterioles. An increased venous pressure causes a proportional increase in filtration through the vessel wall.
- (8) A venopressor mechanism (a pump effect caused by alternate compression and relaxation of muscles surrounding the blood vessels) is believed to exist, which works in conjunction with the valves to return the blood to the heart. A failure in venous return results from the packing of abnormally viscous blood, first, in the venous vessels, then in the capillary network, and last of all in the arterial vessels. A condition of complete stasis is then existent.



- A B S T R A C T -

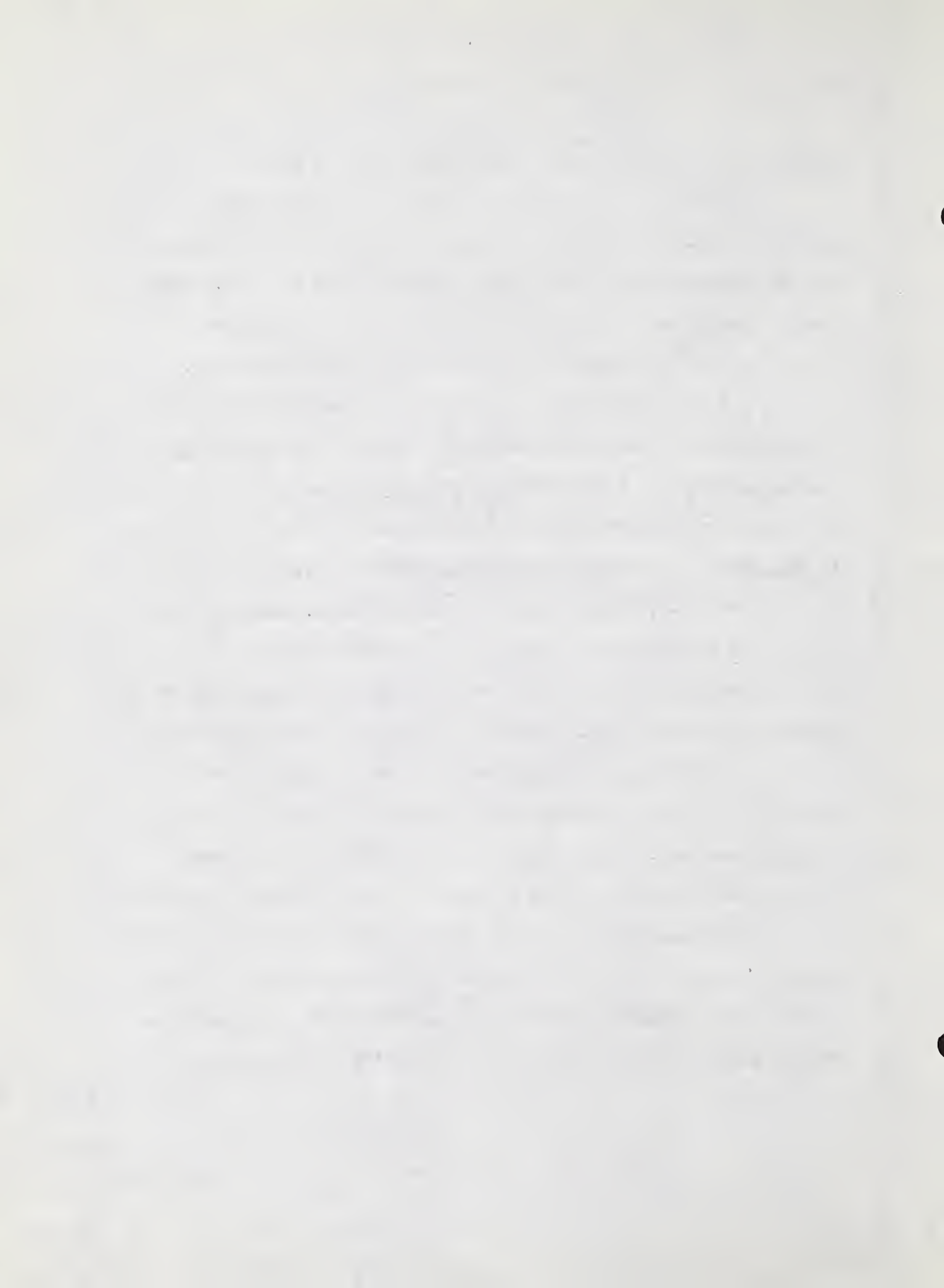
This review of the literature which is written about the veins considers the morphological and the physiological characteristics. The veins, like the arteries, are composed of three layers of tissue. The inner layer of tissue, the endothelium, is a colorless, transparent structure, composed of many cells which are more oval and less fusiform than the endothelial cells of the artery. The function of this tissue is to provide a smooth lining that will not hinder the blood flow. The endothelium of the venules and the venous capillaries has another function. Here, the tissue serves as a semi-permeable membrane to permit the exchange of the body fluids through the vascular wall. The middle layer of tissue is composed chiefly of circular layers of smooth muscle, though much thinner than the smooth muscle layer in the artery. This center layer gives support to the vessel wall and resists the internal pressure. The smooth muscle is regulated by autonomic nervous control and has the capacity to contract and relax. The outer layer, composed of connective tissue, usually occurs as a sheath around the larger veins. It is within this tissue that the vasa vasorum are located. The function of this outer layer is to protect the vessel, to support the vasa vasorum, to isolate the vessel and to aid the

valves by preventing too great a distention of the vessel.

There is a sharp structural difference between the arteriole and the venule. The arteriole has a muscular layer of tissue overlying the endothelial tube, the same as the artery and the vein. The venule, which is very scantily or not at all supplied with muscular tissue, has only the connective tissue overlying the endothelium.

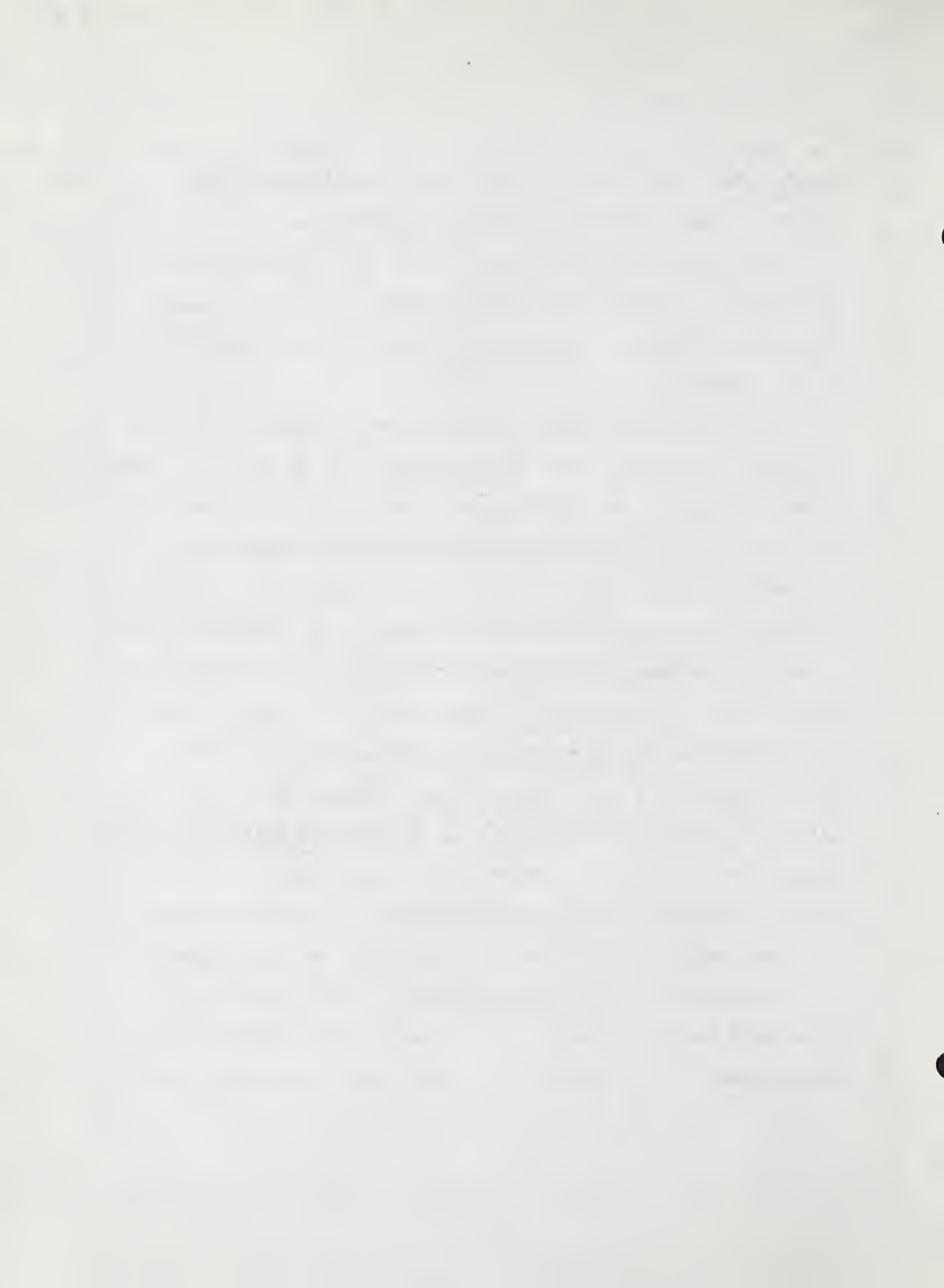
Venous pressure has received most of the attention of the investigators who have studied the veins. By use of the direct method (by cannulation of a vein) or the indirect method (external application of pressure until the vein has collapsed) a fairly accurate figure can be obtained. The average venous pressure in man is found to vary from 30 to 90 mm. of water. Venous pressure is not constant. Local changes in temperature cause a change in the venous pressure. Rigorous muscular activity produces an elevation of venous pressure which gradually rises until fatigue takes place. A change in posture from the recumbent to the erect position produces an elevation of pressure to overcome the hydrostatic factor. A definite rise in pressure, also results with an increase of age. Respiration may have slight affect upon venous pressure; causing a fall during inspiration and a rise during expiration

The smooth muscle of the vein is innervated by nerves from the autonomic nervous system. The presence of sympathetic fibers is confirmed, but no definite evidence has been advanced to prove the existence of parasympathetic fibers. Adrenalin, Parke Davis, produces



constriction of the veins, an action similar to stimulation of the sympathetic nerve. Histamine produces constriction of veins which have a very stout covering of smooth muscle. Small veins are inactive to this drug. Acetylcholine, usually a blood vessel dilator, gives inconsistent results. At one time it may constrict and another time it may dilate.

The venous vessels have a vital part to play in the process of circulation. They are more than passageways for the return of venous blood to the heart. The smaller vessels serve as absorptive surfaces. The venules and the venous capillaries are far more permeable than are the vessels of the arterial side of the circulatory system. A poorly diffusible dye, injected into an artery, will diffuse through the walls of venous capillaries before there is any trace of diffusion through the arterial capillaries. This suggests that much of the filtration (exchange), through the blood vessel wall, takes place in the small venous vessels. The venous capillaries are bare endothelial tubes with minute fenestrae or seep valves through which diffusion takes place. The movement of the blood in the veins is dependent upon arterial pressure, the tonus of the muscle surrounding the vein (venopressor mechanism) and the valves of the vein. A stoppage of the blood in the veins by venous occlusion results in a loss of fluid through the vessel wall into the tissues. Plasma, containing 0.03% protein, passes through first, and some whole blood passes through later. A



condition of stasis results from the packing of erythrocytes in the venules, the capillaries and last of all in the arterioles.

From this survey it is evident that there is definite need for further research to be conducted in this field. If the microscopical and macroscopical features of any particular vein are considered in relation to the properties of the vein wall, to the anatomical and circulatory features of the tissue, and to the innervation and response to autonomic drugs, a fairly accurate estimate of its physiological activity can be obtained.

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